Big Fish Story:
A 39-year old man with extrapulmonary sarcoidosis, acute renal failure, and bilateral pulmonary infiltrates

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HPI

- 39 y.o. M transferred to WRAMC from outside facility for rising creatinine and pulmonary infiltrates.
- 6 years PTA: Extensive w/u of fatigue and elevated liver enzymes led to biopsies of liver and abdominal lymph node revealing noncaseating granulomas. Dx of sarcoidosis m/b granulomatous hepatitis. CXR normal.

HPI (cont.)

- Placed on prolonged steroid taper ending summer 1997 (7 mos. PTA).
- Six mos. PTA: reportedly dx with otitis media, rx with antibioti
- Six weeks PTA: dx with gout in L great toe (presumptive), rx with colchicine + indomethacin x 10 days, then naproxen 500 mg po bid until 4 days PTA.

HPI (cont.)

- 11 days PTA: Cr = 1.3 (in 1993, Cr = 1.2)
- 5 days PTA: ate wild berries with wife. Subsequently both developed dysuria, frequency, dark-colored urine, flank pain. Wife's sxs resolved, his did not.
- 2 days PTA: Dx with UTI at primary care clinic, placed on ciprofloxacin 500 mg po bid without significant improvement.

HPI (cont.)

- 1 day PTA: non-productive cough, DOE, right pleuritic chest pain, chills, myalgias.
- DOA: productive co ith yellow-green sputum (blood-streaked?), fever to 103 ◦F, rigors, nausea/vomiting, brown watery stools.

HPI (cont.)

- Presented to outside hospital with CXR showing bilateral alveolar infiltrates, WBC = 14.8 with bandemia, BUN/Cr = 38/5.4.
- Admitted, place on antibiotic coverage for community-acquired pneumonia, transferred to WRAMC the next day when BUN/Cr = 53/7.9 and oliguric.

Past Medical History

- Sarcoidosis as per HPI
- Hemoglobin SC
- gout (presumed), Dec. 1997
- h/o otitis media, 1997
- s/p L knee surgery 1984
- s/p liver biopsy 1992
- s/p abdominal lymph node biopsy 1992

Medications

- Outpatient: naproxen 500 mg po bid x 1 month, ciprofloxacin 500 mg po bid x 2 days, acetaminophen prn
- On transfer: erythromycin 500 mg iv q 6 hrs, ceftriaxone 1 gm iv q 12 hrs
- Allergies: NKDA

Family and Social History

- +HTN (mother d. 42 stroke). +ASCAD (father d. 56 m.i.). +DM (sister).
- No tobacco. No EtOH since 1989. No illicit drug use.
- Active duty USAF working at NSA. Married, no children.

Review of Systems

- No recent travel, ill contact, animal/insect exposure.
- PPD negative in distant past, no known TB exposure.

Physical Examination

- Young muscular BM in moderate respiratory distress, on non-rebreather face mask, able to complete sentences.
- T 101.4 ◦F, BP 160s/70s, P 130s, R 30s SaO2 97-100% on 100% NRB mask. Height = 1.82 m. Weight = 110 kg.
- Skin: no rashes.
- HEENT/neck: TMs clear, normal.

Physical Examination (cont.)

- Pul: bilateral rales in lower 25% of fields, no rubs.
- Cor: no JVD, tachycardic, no m/r/g.
- Abd: mild R flank and RUQ tenderness. No rebound or organomegaly.
- Ext: no edema, adenopathy. Joints normal.
- Neuro: grossly intact, no flap.

Laboratories

- BUN/Cr = 59/9.7, K = 4.4, HCO_3 = 16, AG = 19.
- Ca/Mg/Phos = 8.1/1.7/3.8, TP/Alb = 7.0/3.3
- AST/ALT = 55/53, AlkPhos/TBili = 198/1.3
- ABG = 7.38/31/79 SaO_2 97% on 100% NRB. Lactate = 0.9
- WBC=12.8, HgB/Hct = 9.7/28.8, MCV = 77, plts=192

Laboratories (cont.)

- U/A (catheter) = amber, 1.019/5.0, large blood, 4+ protein, SSA > 100 mg%.
- urine sediment (catheter) = TNTC RBCs with normal morphology, 0-2 WBCs, few fine granular casts, amorphous urates, no cellular casts or crystals, no lipid bodies.

Other Studies

- EKG = sinus tachycardia, no ischemic changes
- CXR = bilateral patchy alveolar infiltrates, no adenopathy.
- Renal U/S = bilateral 12 cm kidneys, no obstruction or stones, otherwise normal scan.
- Sputum GS = gram-negative rods and gram-positive cocci in chains/pairs/clusters.

Summary of Presentation

- Acute oliguric renal failure
- Bilateral pulmonary infiltrates
- Hypoxemia
- Metabolic anion-gap acidosis
- Leukocytosis
- Microcytic anemia

What is the differential diagnosis and what further diagnostic/therapeutic plans are indicated?

Diagnoses Considered

- Pulmonary-Renal Syndromes
  - Wegener's granulomatosis
  - Goodpasture's syndrome
- Post-infectious RPGN
- NSAID/ drug-induced renal failure +/- pneumonia
- Sarcoidosis +/- pneumonia
- Other: infection (hantavirus, Legionella), hemoglobinopathy

Additional Serologies

- CRP = 29.7
- C3/C4 = normal.
- ANA = negative.
- P-ANCA = negative, C-ANCA = negative.
- Anti-GBM Ab= negative.
- ACE = lost by lab.
- DAT = negative.
- HgB EP = SC
- Sickledex = negative.
- Eval by Hematology: HgB C of no clinical consequence.

Infection Workup

- Blood cultures: multiply negative
- Sputum cultures: negative
- Stool cultures: negative
- Urinary Legionella antigen: negative
- AFB cultures: negative
- HIV, influenza, parainfluenza, hantavirus, mycoplasma, puumala titres negative.

Clinical Course I

- DOA: tx to ICU for monitoring, volume repletion, broad spectrum antibiotics.
- HD1: Intubated for respiratory failure, Swann-Ganz line placed showing first volume overload, then sepsis. Anuria develops. BUN/Cr = 66/10.4. Hemodialysis begins.

Clinical Course I (cont.)

- HD 2-4: Sepsis physiology, pressor-dependent, anuric.
- HD 5: Open renal biopsy performed.

Review of Renal Biopsy Specimens

Biopsy Summary

- Patchy interstitial infiltration with edema.
- Some granulomata.
- Glomeruli essential preserved with mild-to-moderate increase in cellularity.
- Some tubule inflammation and necrosis of epithelium.
- No vasculitis.

Biopsy Summary (cont.)

- EM: Rare subepithelial “hu .
- IF: Mesangial C3 and IgM.
- Special stains for micro-organisms (Ziehl-Neelsen’s, GMS, Warthin-Starry, Brown-Hopps) negative.

Clinical Course II

- HD 6: Fiberoptic bronchoscopy with BAL unrevealing.
- HD 7-9: Methylprednisolone 1 gm IV q day.
- HD 11: Extubated. BUN/Cr = 92/9.4, dialysis #7 performed. Started on prednisone 80 mg po qd.

Clinical Course II (cont.)

- HD15: Dialysis #10 (last) performed.
- HD 16: urine output = 2 liters. BUN/Cr = 86/7.5
- HD 22: BUN/Cr = 83/4.3. Discharged from hospital on slow prednisone taper.
- 40 days post-d/c: BUN/Cr = 19/1.6

Diagnoses

- Acute renal failure secondary to granulomatous interstitial nephritis.
- Community-acquired pneumonia.

Renal Sarcoidosis

- Histological evidence of disease in 7-27% of autopsy reports.
- Clinically evident in 1-5% of patients.
- Disease is most commonly a manifestation of hypercalcemic nephropathy.

Manifestations of Renal Sarcoidosis

- Hypercalcemic nephropathy: nephrolithiasis, nephrocalcinosis, hypercalciuria (with renal vasoconstriction)
- Tubulointerstitial disease: concentrating defects, diabetes insipidus, RTAs, interstitial nephritis with or without granulomas, granulomatous arteritis
- Glomerulonephritis
- Obstruction from retroperitoneal adenopathy

ARF and Sarcoidosis

- “Rare” but several case reports exist.
- Bear *et al.* (1979): 6 cases of renal sarcoid presenting as ARF with interstitial nephritis/tubular atrophy.
- Singh *et al.* (1998): Three case reports of ARF with noncaseating granulomatous interstitial nephritis.
- Steroid-responsive.
- Relapse common when steroids withdrawn.

Lingering Questions

- Etiology of pulmonary process?
- Contributing factor of NSAIDs?
- Significance of subepithelial “humps”?
- Etiology of initial urinary tract symptoms?